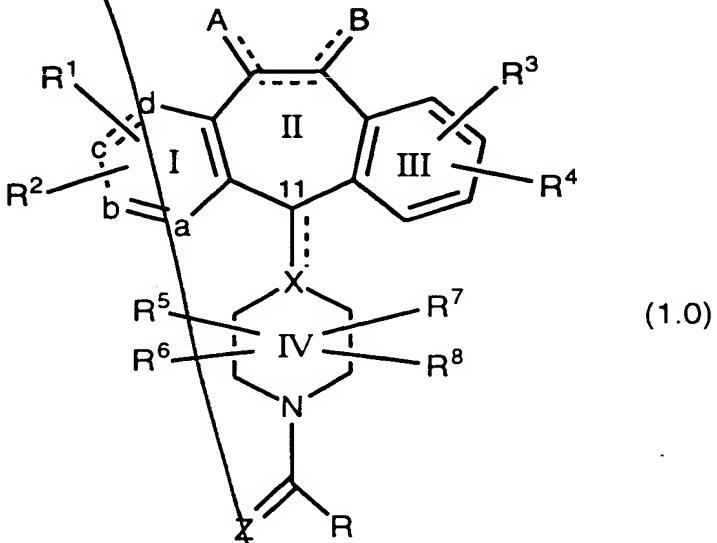


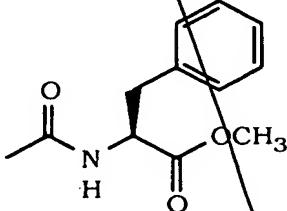
WHAT IS CLAIMED IS:

1. A method for inhibiting the abnormal growth of cells comprising administering an effective amount of a compound of Formula  
5 1.0:



or a pharmaceutically acceptable salt or solvate thereof, wherein:

- one of a, b, c and d represents N or NR<sup>9</sup> wherein R<sup>9</sup> is O<sup>-</sup>, -CH<sub>3</sub> or -(CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>H wherein n is 1 to 3, and the remaining a, b, c and d groups  
10 represent CR<sup>1</sup> or CR<sup>2</sup>; or  
each of a, b, c, and d are independently selected from CR<sup>1</sup> or CR<sup>2</sup>;  
each R<sup>1</sup> and each R<sup>2</sup> is independently selected from H, halo, -CF<sub>3</sub>,  
-OR<sup>10</sup>, -COR<sup>10</sup>, -SR<sup>10</sup>, -S(O)<sub>t</sub>R<sup>11</sup> (wherein t is 0, 1 or 2), -SCN, -N(R<sup>10</sup>)<sub>2</sub>,  
-NO<sub>2</sub>, -OC(O)R<sup>10</sup>, -CO<sub>2</sub>R<sup>10</sup>, -OCO<sub>2</sub>R<sup>11</sup>, -CN, -NHC(O)R<sup>10</sup>, -NHSO<sub>2</sub>R<sup>10</sup>,  
15 -CONHR<sup>10</sup>, -CONHCH<sub>2</sub>CH<sub>2</sub>OH, -NR<sup>10</sup>COOR<sup>11</sup>, -SR<sup>11</sup>C(O)OR<sup>11</sup>,



- SR<sup>11</sup>N(R<sup>75</sup>)<sub>2</sub> (wherein each R<sup>75</sup> is independently selected from H and -C(O)OR<sup>11</sup>), benzotriazol-1-yloxy, tetrazol-5-ylthio, or substituted tetrazol-5-ylthio, alkynyl, alkenyl or alkyl, said alkyl or alkenyl group optionally  
20 being substituted with halo, -OR<sup>10</sup> or -CO<sub>2</sub>R<sup>10</sup>;

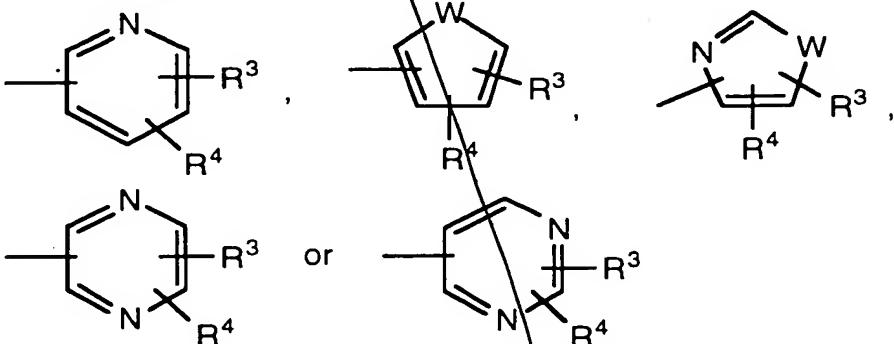
R<sup>3</sup> and R<sup>4</sup> are the same or different and each independently represents H, any of the substituents of R<sup>1</sup> and R<sup>2</sup>, or R<sup>3</sup> and R<sup>4</sup> taken

together represent a saturated or unsaturated C<sub>5</sub>-C<sub>7</sub> fused ring to the benzene ring;

- R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> each independently represents H, -CF<sub>3</sub>, -COR<sup>10</sup>, alkyl or aryl, said alkyl or aryl optionally being substituted with -OR<sup>10</sup>, -SR<sup>10</sup>, -S(O)<sub>t</sub>R<sup>11</sup>, -NR<sup>10</sup>COOR<sup>11</sup>, -N(R<sup>10</sup>)<sub>2</sub>, -NO<sub>2</sub>, -COR<sup>10</sup>, -OCOR<sup>10</sup>, -OCO<sub>2</sub>R<sup>11</sup>, -CO<sub>2</sub>R<sup>10</sup>, OPO<sub>3</sub>R<sup>10</sup> or one of R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> and R<sup>8</sup> can be taken in combination with R<sup>40</sup> as defined below to represent -(CH<sub>2</sub>)<sub>r</sub> wherein r is 1 to 4 which can be substituted with lower alkyl, lower alkoxy, -CF<sub>3</sub> or aryl, or R<sup>5</sup> is combined with R<sup>6</sup> to represent =O or =S and/or R<sup>7</sup> is combined with R<sup>8</sup> to represent =O or =S;
- R<sup>10</sup> represents H, alkyl, aryl, or aralkyl;
- R<sup>11</sup> represents alkyl or aryl;
- X represents N, CH or C, which C may contain an optional double bond, represented by the dotted line, to carbon atom 11;
- the dotted line between carbon atoms 5 and 6 represents an optional double bond, such that when a double bond is present, A and B independently represent -R<sup>10</sup> halo, -OR<sup>11</sup>, -OCO<sub>2</sub>R<sup>11</sup> or -OC(O)R<sup>10</sup>, and when no double bond is present between carbon atoms 5 and 6, A and B each independently represent H<sub>2</sub>, -(OR<sup>11</sup>)<sub>2</sub>; H and halo, dihalo, alkyl and H, (alkyl)<sub>2</sub>, -H and -OC(O)R<sup>10</sup>, H and -OR<sup>10</sup>, =O, aryl and H, =NOR<sup>10</sup> or -O-(CH<sub>2</sub>)<sub>p</sub>-O- wherein p is 2, 3 or 4;

R represents R<sup>40</sup>, R<sup>42</sup>, R<sup>44</sup>, or R<sup>54</sup>, as defined below;

R<sup>40</sup> represents H, aryl, alkyl, cycloalkyl, alkenyl, alkynyl or -D wherein -D represents

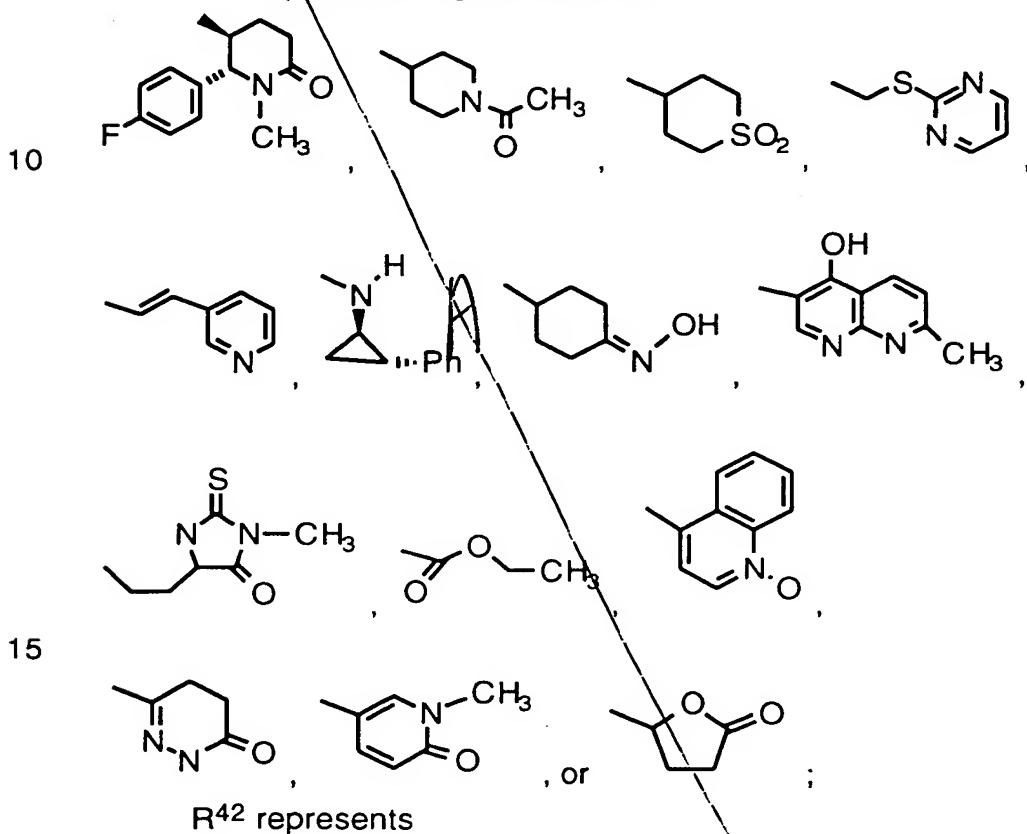


- wherein R<sup>3</sup> and R<sup>4</sup> are as previously defined and W is O, S or NR<sup>10</sup> wherein R<sup>10</sup> is as defined above; said R<sup>40</sup> cycloalkyl, alkenyl and alkynyl groups being optionally substituted with from 1-3 groups selected from halo, -CON(R<sup>10</sup>)<sub>2</sub>, aryl, -CO<sub>2</sub>R<sup>10</sup>, -OR<sup>12</sup>, -SR<sup>12</sup>, -N(R<sup>10</sup>)<sub>2</sub>, -N(R<sup>10</sup>)CO<sub>2</sub>R<sup>11</sup>, -COR<sup>12</sup>, -NO<sub>2</sub> or D, wherein -D, R<sup>10</sup> and R<sup>11</sup> are as

defined above and R<sup>12</sup> represents R<sup>10</sup>, -(CH<sub>2</sub>)<sub>m</sub>OR<sup>10</sup> or -(CH<sub>2</sub>)<sub>q</sub>CO<sub>2</sub>R<sup>10</sup> wherein R<sup>10</sup> is as previously defined, m is 1 to 4 and q is 0 to 4; said alkenyl and alkynyl R<sup>40</sup> groups not containing -OH, -SH or -N(R<sup>10</sup>)<sub>2</sub> on a carbon containing a double or triple bond respectively; or

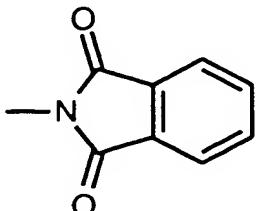
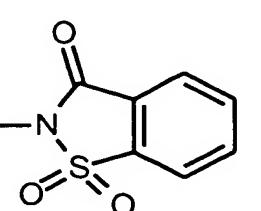
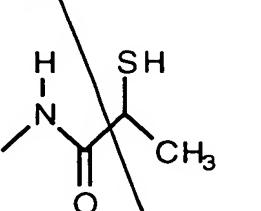
5 R<sup>40</sup> represents phenyl substituted with a group selected from -SO<sub>2</sub>NH<sub>2</sub>, -NSO<sub>2</sub>CH<sub>3</sub>, -SO<sub>2</sub>NHCH<sub>3</sub>, -SO<sub>2</sub>CH<sub>3</sub>, -SOCH<sub>3</sub>, -SCH<sub>3</sub>, or -NSO<sub>2</sub>CF<sub>3</sub>, preferably, said group is located in the para position of the phenyl ring; or

R<sup>40</sup> represents a group selected from



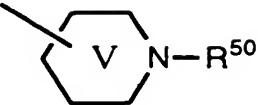
wherein R<sup>20</sup>, R<sup>21</sup> and R<sup>46</sup> are each independently selected from the  
20 group consisting of:

- (1) H;
- (2) -(CH<sub>2</sub>)<sub>q</sub>SC(O)CH<sub>3</sub> wherein q is 1 to 3;
- (3) -(CH<sub>2</sub>)<sub>q</sub>OSO<sub>2</sub>CH<sub>3</sub> wherein q is 1 to 3;
- (4) -OH;

- (5)  $-\text{CS}(\text{CH}_2)_w$ (substituted phenyl) wherein w is 1 to 3 and the substituents on said substituted phenyl group are the same substituents as described below for said substituted phenyl;
- (6)  $-\text{NH}_2$ ;
- 5 (7)  $-\text{NHCBZ}$ ;
- (8)  $-\text{NHC(O)OR}^{22}$  wherein  $\text{R}^{22}$  is an alkyl group having from 1 to 5 carbon atoms, or  $\text{R}^{22}$  represents phenyl substituted with 1 to 3 alkyl groups;
- (9) alkyl;
- 10 (10)  $-(\text{CH}_2)_k$ phenyl wherein k is 1 to 6;
- (11) phenyl;
- (12) substituted phenyl wherein the substituents are selected from the group consisting of, halo,  $\text{NO}_2$ ,  $-\text{OH}$ ,  $-\text{OCH}_3$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{22}$ ,  $-\text{N}(\text{R}^{22})_2$ , alkyl,  $-\text{O}(\text{CH}_2)_t$ phenyl (wherein t is from 1 to 3), and  $-\text{O}(\text{CH}_2)_t$ substituted phenyl (wherein t is from 1 to 3);
- (13) naphthyl;
- 15 (14) substituted naphthyl, wherein the substituents are as defined for substituted phenyl above;
- (15) bridged polycyclic hydrocarbons having from 5 to 10 carbon atoms;
- 20 (16) cycloalkyl having from 5 to 7 carbon atoms;
- (17) heteroaryl;
- (18) hydroxyalkyl;
- (19) substituted pyridyl or substituted pyridyl N-oxide wherein the substituents are selected from methylpyridyl, morpholinyl, imidazolyl, 1-piperidinyl, 1-(4-methylpiperazinyl),  $-\text{S(O)}_t\text{R}^{11}$ , or any of the substituents given above for said substituted phenyl, and said substituents are bound to a ring carbon by replacement of the hydrogen bound to said carbon;
- 25 (20)
- 
- (21)
- 
- (22)
- 
- 30 (23)  $-\text{NHC(O)}-(\text{CH}_2)_k$ -phenyl or  $-\text{NH(O)-(CH}_2)_k$ -substituted phenyl, wherein said k is as defined above;

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(24) piperidine Ring V:



wherein R<sup>50</sup> represents H, alkyl, alkyloxycarbonyl, alkyloxy carbonyl, haloalkyl, or -C(O)NH(R<sup>10</sup>) wherein R<sup>10</sup> is H or alkyl;

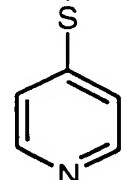
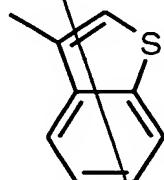
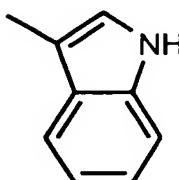
5 (25) -NHC(O)CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub> or -NHC(O)CH<sub>2</sub>-substituted-C<sub>6</sub>H<sub>5</sub>;

(26) -NHC(O)OC<sub>6</sub>H<sub>5</sub>;

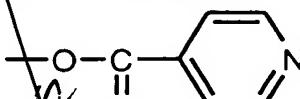
(27)

(28)

(29)



(30) -OC(O)-heterocaryl, for example



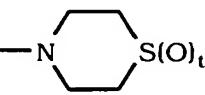
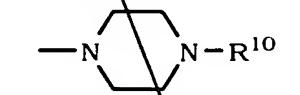
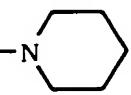
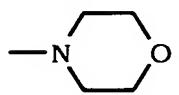
;

10 (31) -O-alkyl (e.g., -OCH<sub>3</sub>); and

(32) -CF<sub>3</sub>;

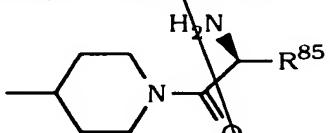
(33) -CN;

(34) a heterocycloalkyl group of the formula



; and

15 (35) a piperidinyl group of the formula

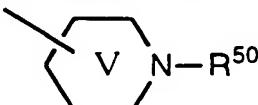


wherein R<sup>85</sup> is H, alkyl, or alkyl substituted by -OH or -SCH<sub>3</sub>; or

R<sup>20</sup> and R<sup>21</sup> taken together form a =O group and the remaining

20 R<sup>46</sup> is as defined above; or

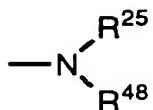
Two of R<sup>20</sup>, R<sup>21</sup> and R<sup>46</sup> taken together form piperidine Ring V



wherein R<sup>50</sup> is as defined above;

with the proviso that R<sup>46</sup>, R<sup>20</sup> and R<sup>21</sup> are selected such that the carbon atom to which they are bound does not contain more than one heteroatom;

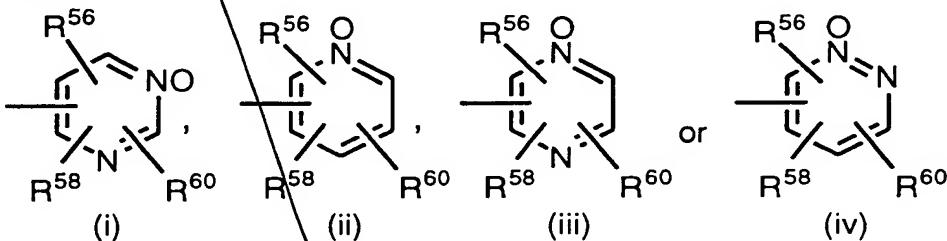
5 R<sup>44</sup> represents



wherein R<sup>25</sup> represents heteroaryl, N-methylpiperidinyl or aryl; and R<sup>48</sup> represents H or alkyl;

R<sup>54</sup> represents an N-oxide heterocyclic group of the formula (i), (ii),

10 (iii) or (iv):

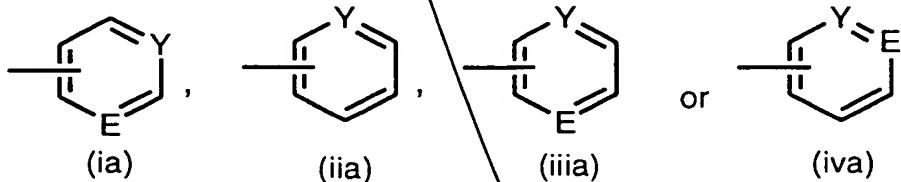


wherein R<sup>56</sup>, R<sup>58</sup>, and R<sup>60</sup> are the same or different and each is independently selected from H, halo, -CF<sub>3</sub>, -OR<sup>10</sup>, -C(O)R<sup>10</sup>, -SR<sup>10</sup>, -S(O)eR<sup>11</sup> (wherein e is 1 or 2), -N(R<sup>10</sup>)<sub>2</sub>, -NO<sub>2</sub>, -CO<sub>2</sub>R<sup>10</sup>, -OCO<sub>2</sub>R<sup>11</sup>,

15 -OCOR<sup>10</sup>, alkyl, aryl, alkenyl or alkynyl, which alkyl may be substituted with -OR<sup>10</sup>, -SR<sup>10</sup> or -N(R<sup>10</sup>)<sub>2</sub> and which alkenyl may be substituted with OR<sup>11</sup> or SR<sup>11</sup>; or

R<sup>54</sup> represents an N-oxide heterocyclic group of the formula (ia),

(iia), (iiiia) or (iva):



20

wherein Y represents N<sup>+</sup>-O<sup>-</sup> and E represents N; or

R<sup>54</sup> represents an alkyl group substituted with one of said N-oxide heterocyclic groups (i), (ii), (iii), (iv), (ia), (iia), (iiiia) or (iva);

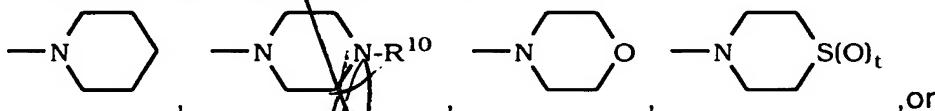
Z represents O or S such that R can be taken in combination with

25 R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup> or R<sup>8</sup> as defined above, or R represents R<sup>40</sup>, R<sup>42</sup>, R<sup>44</sup> or R<sup>54</sup>.

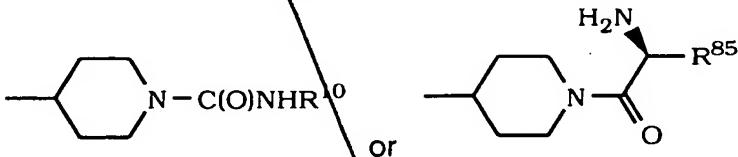
2. The method of Claim 1 wherein a is N and b, c, and d are carbon; R<sup>1</sup> and R<sup>2</sup> are the same or different and each is independently

selected from H, halo, -CF<sub>3</sub>, lower alkyl, or benzotriazol-1-yloxy, and R<sup>1</sup> is at the C-4 position and R<sup>2</sup> is at the C-3 position; R<sup>3</sup> and R<sup>4</sup> are the same or different and each is independently selected from H or halo, and R<sup>3</sup> is at the C-8 position and R<sup>4</sup> is at the C-9 position; when the double bond between carbon atoms 5 and 6 is present, A and B independently represent H, lower alkyl or alkyloxy; and when the double bond between carbon atoms 5 and 6 is absent, A and B independently represent H<sub>2</sub>, (-H and -OH) or =O; R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> are H; Z is O; and R represents R<sup>42</sup> and the R<sup>46</sup> is selected from phenyl, substituted phenyl, heteroaryl or piperidine Ring V.

3. The method of Claim 2 wherein R<sup>20</sup> and R<sup>21</sup> are each independently selected from H and alkyl; R<sup>3</sup> is Cl; R<sup>4</sup> is H; R<sup>1</sup> and R<sup>2</sup> are individually selected from H, benzotriazol-1-yloxy, C<sub>1</sub> to C<sub>4</sub> alkyl or halo; and R<sup>46</sup> represents 3-pyridyl, 3-pyridyl N-oxide, triazolyl, 4-pyridyl, 4-pyridyl N-oxide, 3-N-methylpiperidinyl, 4-N-methylpiperidinyl, 3-N-acetyl piperidinyl, 4-N-acetyl piperidinyl, 1-N-methylpiperazinyl, 1-piperazinyl, a heterocycloalkyl of the formula

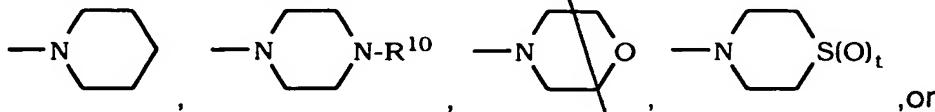


20 a piperidinyl group of the formula

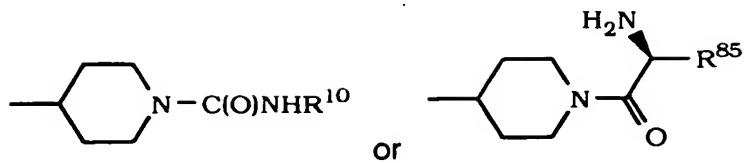


or

4. The method of Claim 3 wherein both R<sup>20</sup> and R<sup>21</sup> are H, or both R<sup>20</sup> and R<sup>21</sup> are methyl; R<sup>1</sup> and R<sup>2</sup> are individually selected from H, Br, Cl, methyl or benzotriazol-1-yloxy; and R<sup>46</sup> represents 3-pyridyl, 3-pyridyl N-oxide, triazolyl, 4-pyridyl, 4-pyridyl N-oxide, 3-N-methylpiperidinyl or 4-N-methylpiperidinyl, 1-N-methylpiperazinyl, 1-piperazinyl, a heterocycloalkyl of the formula



30 a piperidinyl group of the formula



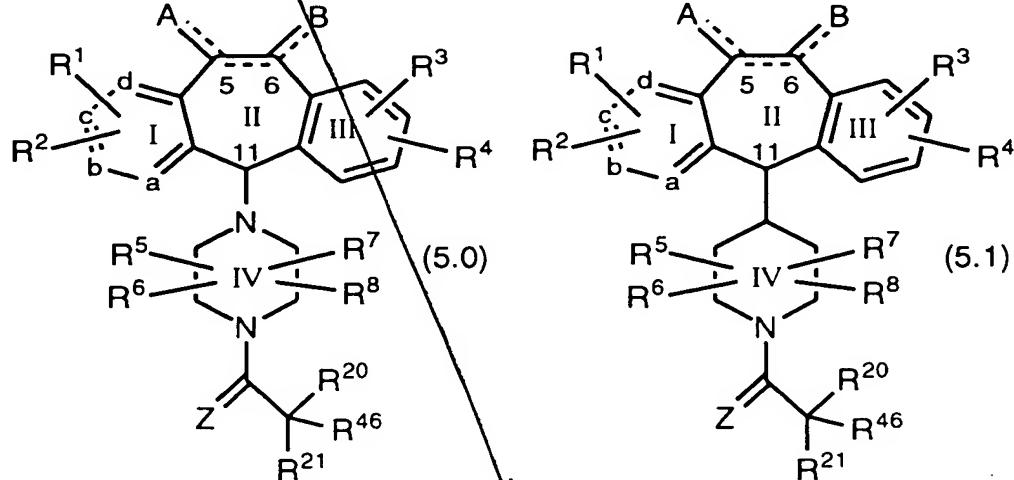
5. The method of Claim 1 wherein a is N and b, c, and d are carbon; R<sup>1</sup> and R<sup>2</sup> are the same or different and each is independently selected from H, halo, -CF<sub>3</sub>, lower alkyl, or benzotriazol-1-yloxy, and R<sup>1</sup> is at the C-4 position and R<sup>2</sup> is at the C-3 position; R<sup>3</sup> and R<sup>4</sup> are the same or different and each is independently selected from H or halo, and R<sup>3</sup> is at the C-8 position and R<sup>4</sup> is at the C-9 position; when the double bond between carbon atoms 5 and 6 is present, A and B independently represent H, lower alkyl or alkyloxy; and when the double bond between carbon atoms 5 and 6 is absent, A and B independently represent H<sub>2</sub>, (-H and -OH) or =O; R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> are H; Z is O; and R represents R<sup>44</sup> and the R<sup>25</sup> represents pyridyl, pyridyl N-oxide, phenyl, 3-N-methylpiperidinyl or 4-N-methylpiperidinyl.
- 10
- 15
6. The method of Claim 5 wherein R<sup>25</sup> represents 3-pyridyl or phenyl; R<sup>3</sup> is Cl; R<sup>4</sup> is H; R<sup>48</sup> represents are H or methyl; and R<sup>1</sup> and R<sup>2</sup> are individually selected from H, benzotriazol-1-yloxy, C<sub>1</sub> to C<sub>4</sub> alkyl or halo.
- 20
7. The method of Claim 6 wherein R<sup>1</sup> and R<sup>2</sup> are individually selected from H, Br, Cl, methyl or benzotriazol-1-yloxy.
- 25
8. The method of Claim 1 wherein the the cells inhibited are tumor cells expressing an activated ras oncogene.
- 30
9. The method of Claim 8 wherein the cells inhibited are pancreatic tumor cells, lung cancer cells, myeloid leukemia tumor cells, thyroid follicular tumor cells, myelodysplastic tumor cells, epidermal carcinoma tumor cells, bladder carcinoma tumor cells or colon tumors cells.
- 35
10. The method of Claim 1 wherein the inhibition of the abnormal growth of cells occurs by the inhibition of ras farnesyl protein transferase.

11. The method of Claim 1 wherein the inhibition is of tumor cells wherein the Ras protein is activated as a result of oncogenic mutation in genes other than the Ras gene.

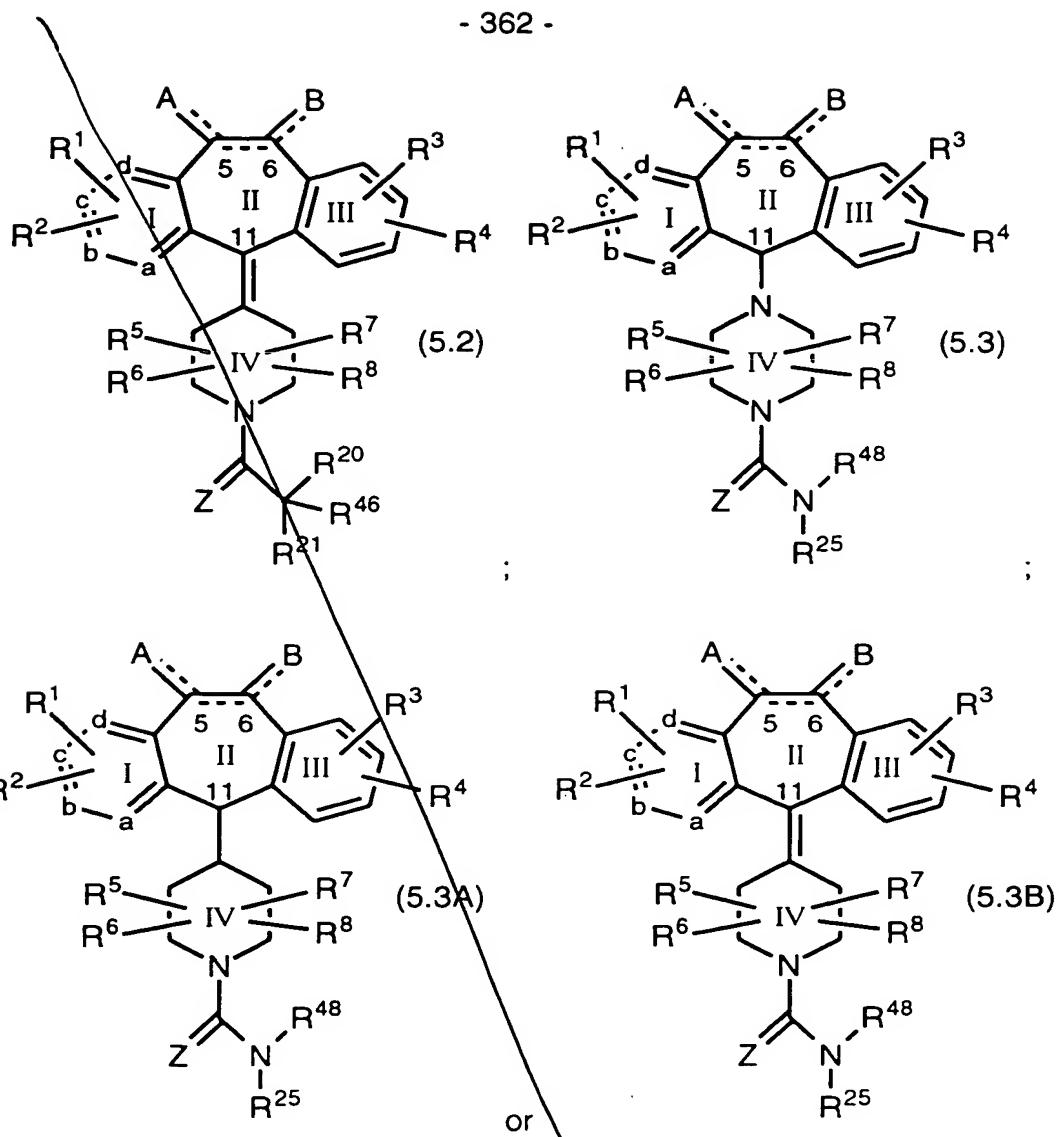
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12. The method of Claim 1 wherein the compound is selected from the compounds of Examples: 1, 2, 3, 4, 5, 6, 19, 42, 43, 44, 45, 46, 47, 48, 49, 75, 76, 78, 82, 83, 84, 85, 89, 121, 180, 182, 183, 184, 187  
10 structure 6.7, 187 structure 6.8, 192, 196, 197, 198, 200, 201, 206, 222,  
223, 224, 225, 226, 227, 233, 234, 236, 239, 246, 247, 248, 249, 250, 251,  
261, 262, 266, 267, 269, 273, 276, 283, 285, 286, 287, 288, 289, 291, 292,  
293, 299, 300, 301, 303, 307, 309, 311, 312, 313, 314, 316, 350, 351, 352,  
354, 356, 426, 400-G, 400-C, 400-F, 400-E, 425-H, 401, 400-B, 400,  
400-L, 425-U, 413, 400-J, 417-B, 438, 411-W, 425-O, 400-D, 400-K,  
15 410-G or 400-H.

13. A compound selected from a compound of the formula:



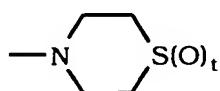
*Sub  
A1*



- or a pharmaceutically acceptable salt or solvate thereof, wherein all the substituents are as defined in Claim 1, and wherein for the compounds of Formula 5.2 the substituents  $R^{20}$ ,  $R^{21}$ , and  $R^{46}$  are selected such that when one of said substituents  $R^{20}$ ,  $R^{21}$ , and  $R^{46}$  is selected from the group consisting of: (1) H, (4) -OH, (6) -NH<sub>2</sub>, (8) -NHC(O)OR<sup>22</sup>, (9) alkyl, (11) phenyl, (17) heteroaryl, (18) hydroxyalkyl, (19) substituted pyridyl, (12) substituted phenyl and (31) -O-alkyl, then the remaining two of said substituents  $R^{20}$ ,  $R^{21}$  and  $R^{46}$  cannot both be H when: (a)  $R^1$  and  $R^2$  are both H, and (b) the double bond between C-5 and C-6 is absent, and (c) both A and B are H<sub>2</sub>, and (d)  $R^4$  is H, and (e)  $R^3$  is H or Cl at C-8.

- 15        14. The compound of Claim 13 wherein a is N and b, c, and d are carbon;  $R^1$  and  $R^2$  are the same or different and each is independently selected from H, halo, -CF<sub>3</sub>, lower alkyl, or benzotriazol-1-

- yloxy, and R<sup>1</sup> is at the C-4 position and R<sup>2</sup> is at the C-3 position; R<sup>3</sup> and R<sup>4</sup> are the same or different and each is independently selected from H or halo, and R<sup>3</sup> is at the C-8 position and R<sup>4</sup> is at the C-9 position; when the double bond between carbon atoms 5 and 6 is present, A and B
- 5    independently represent H, lower alkyl or alkyloxy; and when the double bond between carbon atoms 5 and 6 is absent, A and B independently represent H<sub>2</sub>, (-H and -OH) or =O; R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> are H; Z is O; and R<sup>46</sup> is selected from phenyl, substituted phenyl, heteroaryl, piperidine Ring V, 1-N-methylpiperazinyl, 1-piperazinyl or a heterocycloalkyl of the
- 10   formula

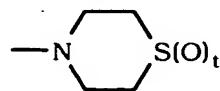


- 15   15. The compound of Claim 14 wherein R<sup>20</sup> and R<sup>21</sup> are each independently selected from H and alkyl; R<sup>3</sup> is Cl; R<sup>4</sup> is H; R<sup>1</sup> and R<sup>2</sup> are individually selected from H, benzotriazol-1-yloxy, C<sub>1</sub> to C<sub>4</sub> alkyl or halo; and R<sup>46</sup> represents 3-pyridyl, 3-pyridyl N-oxide, 4-pyridyl, 4-pyridyl N-oxide, 3-N-methylpiperidinyl, 4-N-methylpiperidinyl, 3-N-acetyl piperidinyl, 4-N-acetyl piperidinyl, 1-N-methylpiperazinyl, 1-piperazinyl or a heterocycloalkyl of the formula



20

- 25   16. The compound of Claim 15 wherein both R<sup>20</sup> and R<sup>21</sup> are H, or both R<sup>20</sup> and R<sup>21</sup> are methyl; R<sup>1</sup> and R<sup>2</sup> are individually selected from H, Br, Cl, methyl or benzotriazol-1-yloxy; and R<sup>46</sup> represents 3-pyridyl, 3-pyridyl N-oxide, triazolyl, 4-pyridyl, 4-pyridyl N-oxide, 3-N-methylpiperidinyl, 4-N-methylpiperidinyl, 1-N-methylpiperazinyl, 1-piperazinyl or a heterocycloalkyl of the formula



30

17. The compound of Claim 13 wherein a is N and b, c, and d are carbon; R<sup>1</sup> and R<sup>2</sup> are the same or different and each is independently selected from H, halo, -CF<sub>3</sub>, lower alkyl, or benzotriazol-1-yloxy, and R<sup>1</sup> is at the C-4 position and R<sup>2</sup> is at the C-3 position; R<sup>3</sup> and

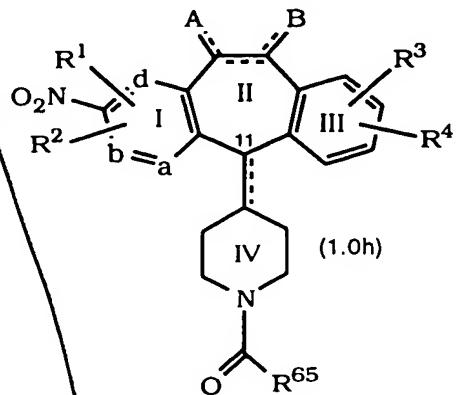
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- R<sup>4</sup> are the same or different and each is independently selected from H or halo, and R<sup>3</sup> is at the C-8 position and R<sup>4</sup> is at the C-9 position; when the double bond between carbon atoms 5 and 6 is present, A and B independently represent H, lower alkyl or alkyloxy; and when the double bond between carbon atoms 5 and 6 is absent, A and B independently represent H<sub>2</sub>, (-H and -OH) or =O; R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> are H; Z is O; and R<sup>25</sup> represents phenyl, 3-pyridyl, 3-pyridyl N-oxide, 4-pyridyl, 4-pyridyl N-oxide, 3-N-methylpiperidinyl, 4-N-methylpiperidinyl, 3-N-acetyl piperidinyl or 4-N-acetyl piperidinyl.
- 10            18. The compound of Claim 17 wherein R<sup>25</sup> represents phenyl, 3-pyridyl, 3-pyridyl N-oxide, 4-pyridyl, 4-pyridyl N-oxide, 3-N-methylpiperidinyl or 4-N-methylpiperidinyl; R<sup>3</sup> is Cl; R<sup>4</sup> is H; R<sup>48</sup> represents are H or methyl; and R<sup>1</sup> and R<sup>2</sup> are individually selected from H, benzotriazol-1-yloxy, C<sub>1</sub> to C<sub>4</sub> alkyl or halo.
- 15            19. The compound of Claim 18 wherein R<sup>1</sup> and R<sup>2</sup> are individually selected from H, Br, Cl, methyl or benzotriazol-1-yloxy.
- 20            20. The compound of Claim 13 selected from a compound having the structure number: 5.17, 5.18, 5.19, 5.20, 5.21, 5.22, 5.23, 5.60, 5.61, 5.62, 5.63, 5.64, 5.65, 5.66, 5.67, 5.68, 5.69, 5.70, 5.71, 5.72, 5.73, 5.74, 5.75, 5.76, 5.77, 5.78, 5.79, 5.81, 5.82, 5.83, 5.84, 5.85, 5.90, 5.91, 5.96, 5.97, 5.98, 5.99, 5.100, 5.101, 5.108, 5.109, 5.110, 5.111, 5.138, 5.139, 5.140, 5.141, 5.143, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 5.10, 5.11, 5.12, 5.13, 5.14, 5.15, 5.16, 5.24, 5.26, 5.27, 5.29, 5.30, 5.31, 5.32, 5.33, 5.34, 5.35, 5.36, 5.37, 5.38, 5.40, 5.42, 5.44, 5.45, 5.46, 5.48, 5.92, 5.93, 5.94, 5.95, 5.102, 5.103, 5.104, 5.105, 5.107, 5.114, 5.115, 5.121, 5.122, 5.123, 5.124, 5.125, 5.126, 5.127, 5.128, 5.129, 5.132, 5.133, 5.134, 5.135, 5.136, 5.145, 5.146, 5.147, 5.149, 5.150, 5.151, 5.152, 5.153, 5.154, 5.200, 5.201, 5.202, 5.203, 5.204, 5.205, 5.206, 5.207, 5.208, 5.209, 5.210, 5.211, 5.212, 5.213, 5.214, 5.215, 5.216, 5.217, 5.218, 5.219, 5.220, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 6.10, 6.11, 6.17, 6.19, 6.12, 6.13 or 6.14; or selected from the compound of example number 82, 82A, 235, 316, 323, 310, 350, 352, 355, 89, 180, 181, 204, 234, 287, 288, 289, 290, 295, 296, 297, 298, 299, 300, 301, 303, 304, 305, 307, 309, 311, 356, 312, 313, 314, 354, 291, 292, 293 or 294 .

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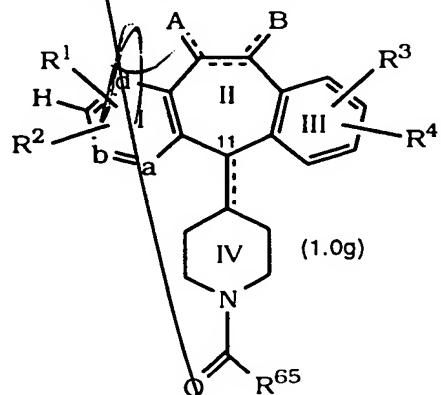
21. A pharmaceutical composition for inhibiting the abnormal growth of cells comprising an effective amount of compound of Claim 13 in combination with a pharmaceutically acceptable carrier.

- 5        22. A process for producing 3-nitro substituted compounds of  
Formula 1.0h:



wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, A, B, a, b, d, and the dotted lines are as defined for Formula 1.0 in Claim 1, and R<sub>65</sub> represents H or -OR<sub>66</sub> wherein R<sub>66</sub> represents alkyl, comprising:

reacting one molar equivalent of a compound of Formula 1.0g:

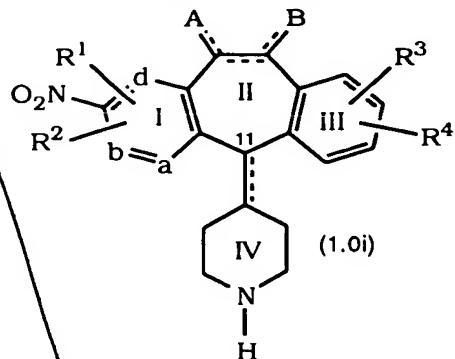


wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, A, B, a, b, d, and the dotted lines are as defined for Formula 1.0 in Claim 1, and R<sub>65</sub> represents H or -OR<sub>66</sub> wherein R<sub>66</sub> represents alkyl;

with one molar equivalent of a nitrating reagent, said nitrating reagent being preformed by mixing, at cold temperature, equimolar amounts of tetrabutyl ammonium nitrate with TFAA;  
the reaction of said nitrating reagent with said compound of  
20 Formula 1.0g taking place in a suitable aprotic solvent; and  
said reaction with said nitrating reagent being conducted at a  
temperature and for a period of time sufficient to allow the reaction to

proceed at a reasonable rate to produce the 3-nitro compound of Formula 1.0h.

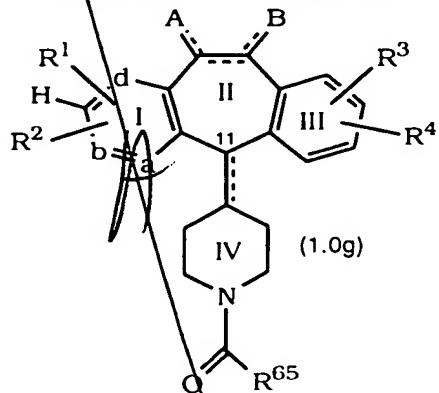
23. A process for producing 3-nitro compounds of the formula:



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wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, A, B, a, b, d, and the dotted lines are as defined for Formula 1.0 in Claim 1, comprising:

reacting one molar equivalent of a compound of Formula 1.0g;

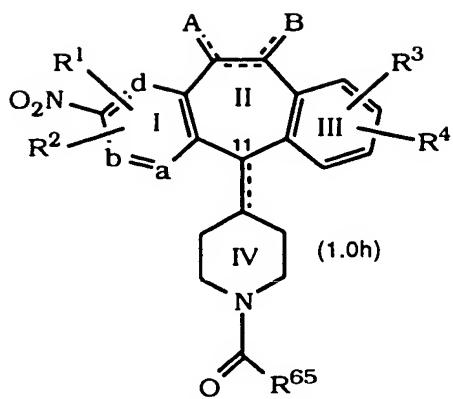


10 wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, A, B, a, b, d, and the dotted lines are as defined for Formula 1.0 in Claim 1, and R<sup>65</sup> represents H or -OR<sup>66</sup> wherein R<sup>66</sup> represents alkyl;

15 with one molar equivalent of a nitrating reagent, said nitrating reagent being preformed by mixing, at cold temperature, equimolar amounts of tetrabutyl ammonium nitrate with TFAA;

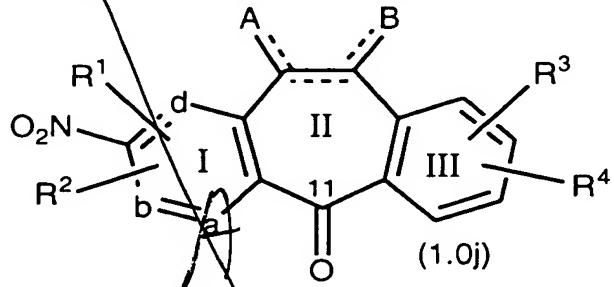
the reaction of said nitrating reagent with said compound of Formula 1.0g taking place in a suitable aprotic solvent; and

20 said reaction with said nitrating reagent being conducted at a temperature and for a period of time sufficient to allow the reaction to proceed at a reasonable rate to produce the 3-nitro compound of Formula 1.0h:



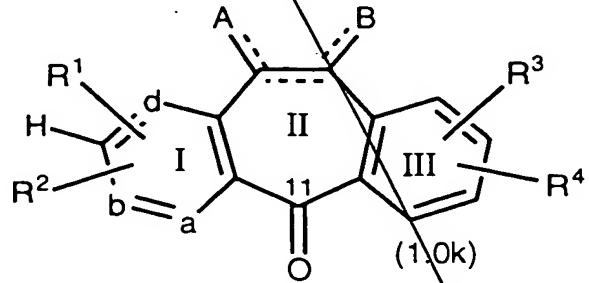
hydrolyzing the compound of Formula 1.0h by dissolving the compound of Formula 1.0h in a sufficient amount of concentrated acid, and heating the resulting mixture to a temperature sufficient to remove the 5 -C(O)R<sup>65</sup> substituent to produce the compound of Formula 1.0i.

24. A process for producing compounds of the formula:



wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, A, B, a, b, d, and the dotted lines are as defined for 10 Formula 1.0 in Claim 1, comprising:

reacting one molar equivalent a compound of formula:



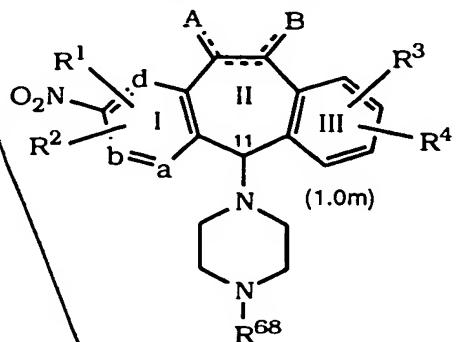
with one molar equivalent of a nitrating reagent; 15 said nitrating reagent being preformed, by mixing at a cold temperature, equimolar amounts of tetrabutyl ammonium nitrate with TFAA;

the reaction of said nitrating reagent with the compound of Formula 1.0k taking place in a suitable aprotic solvent;

said reaction with said nitrating reagent being conducted at a temperature and for a period of time sufficient to allow the reaction to proceed at a reasonable rate to produce the 3-nitro compound of Formula 1.0j.

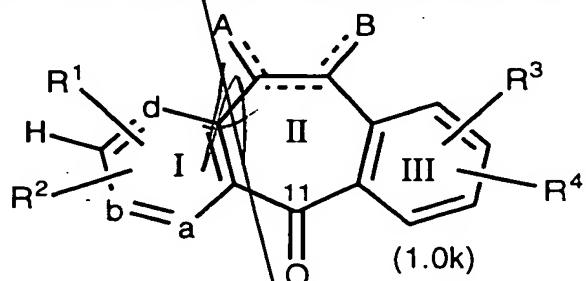
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25. A process for producing a compound of Formula 1.0m:



wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, A, B, a, b, d, and the dotted lines are as defined for Formula 1.0 in Claim 1, and wherein R<sup>68</sup> is H or -COOR<sup>a</sup> wherein R<sup>a</sup> is a C<sub>1</sub> to C<sub>3</sub> alkyl group, comprising:

10 reacting one molar equivalent a compound of formula:

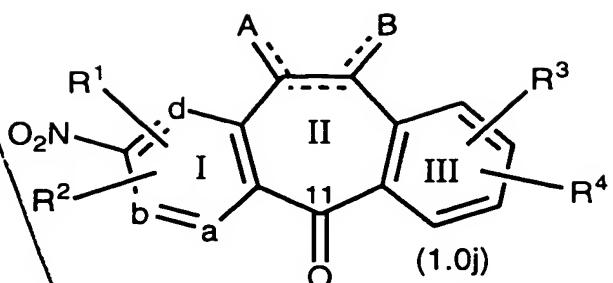


with one molar equivalent of a nitrating reagent;

15 said nitrating reagent being preformed, by mixing at a cold temperature, equimolar amounts of tetrabutyl ammonium nitrate with TFAA;

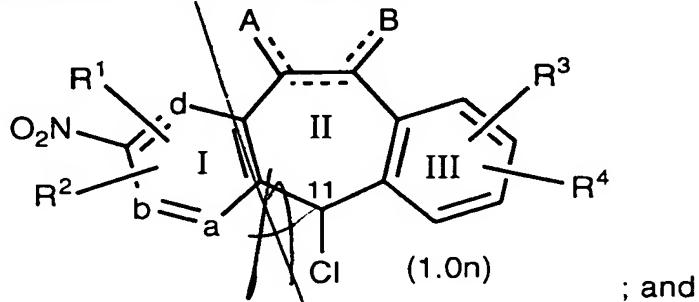
the reaction of said nitrating reagent with the compound of Formula 1.0k taking place in a suitable aprotic solvent;

20 said reaction with said nitrating reagent being conducted at a temperature and for a period of time sufficient to allow the reaction to proceed at a reasonable rate to produce the 3-nitro compound of Formula 1.0j:

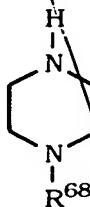


reducing said compound of Formula 1.0j with a suitable reducing agent in a suitable solvent at a suitable temperature to allow the reaction to proceed at a reasonable rate;

- 5 reacting the resulting hydroxy product with a chlorinating agent in a suitable organic solvent at a suitable temperature to allow the reaction to proceed at a reasonable rate to produce a compound of Formula 1.0n;

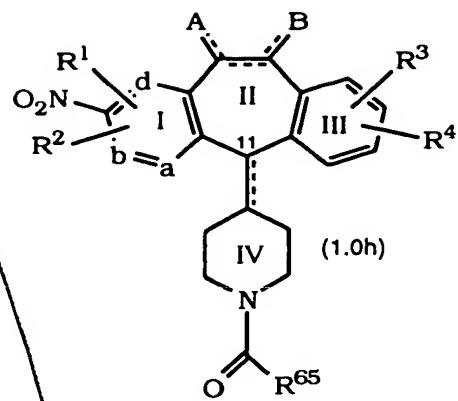


reacting said compound of Formula 1.0n with a compound of the formula:

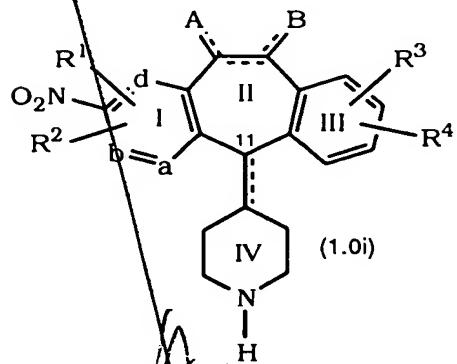


wherein R<sup>68</sup> is as previously defined, in a suitable organic solvent containing a suitable base at a suitable temperature to allow the reaction to proceed at a reasonable rate to produce the compounds of Formula 1.0m.

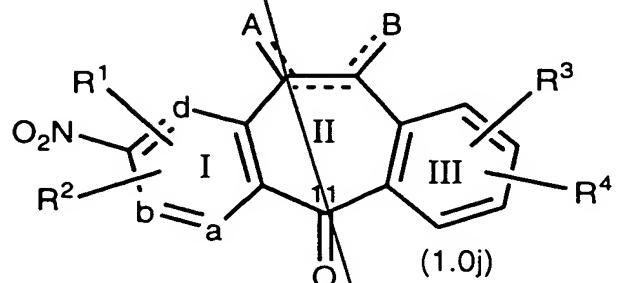
26. A compound selected from a compound of the formula:



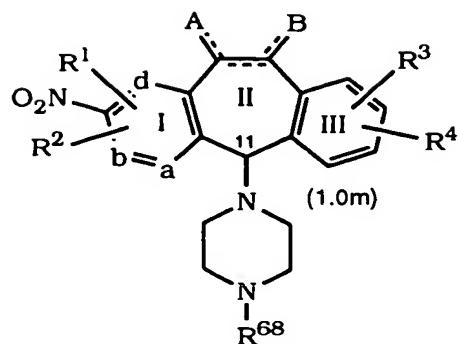
wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{A}$ ,  $\text{B}$ ,  $\text{a}$ ,  $\text{b}$ ,  $\text{d}$ , and  $\text{R}^{65}$  are as defined for Formula 1.0h in Claim 22;



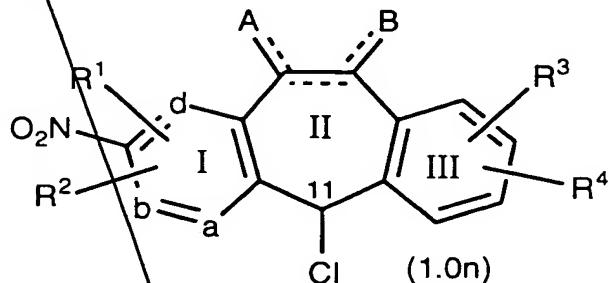
- 5 wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{A}$ ,  $\text{B}$ ,  $\text{a}$ ,  $\text{b}$ , and  $\text{d}$  are as defined for Formula 1.0i in Claim 23;



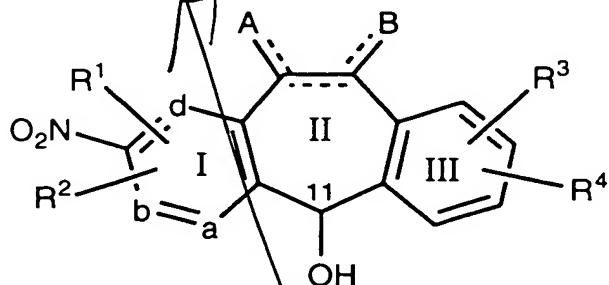
wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{A}$ ,  $\text{B}$ ,  $\text{a}$ ,  $\text{b}$ , and  $\text{d}$  are as defined for Formula 1.0j in Claim 24;



wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, A, B, a, b, d and R<sup>68</sup> are as defined for Formula 1.0m in Claim 25;



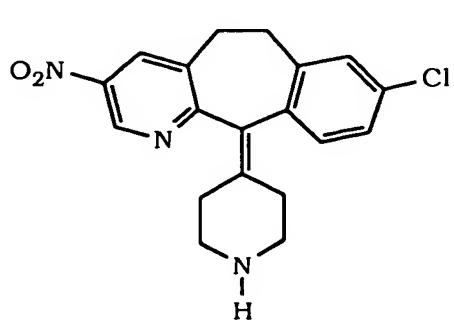
- 5 wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, A, B, a, b, and d are as defined for Formula 1.0j in Claim 24; or



wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, A, B, a, b, and d are as defined for Formula 1.0j in Claim 24.

10

27. A compound selected from a compound of the formula:



or

